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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/786,400	02/24/2004	Alexander William Oxford	56476-DIV2 (71661)	2879
21874	7590	05/01/2007		
EDWARDS ANGELL PALMER & DODGE LLP			EXAMINER	
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			ART UNIT	PAPER NUMBER
			1624	
				MAIL DATE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)
	10/786,400	OXFORD ET AL.
	Examiner	Art Unit
	Tamthom N. Truong	1624

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 06 February 2007.
- 2a) This action is FINAL. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 43-48 and 51-63 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) Claim(s) 44,45 and 60-63 is/are allowed.
- 6) Claim(s) 43,46-48 and 51-59 is/are rejected.
- 7) Claim(s) _____ is/are objected to.
- 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) All b) Some * c) None of:
1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) Notice of References Cited (PTO-892)
- 2) Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____.
- 4) Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) Notice of Informal Patent Application
- 6) Other: _____.

FINAL ACTION

Applicant's amendment of 2-6-07 has been fully considered. The amended claims have overcome the previous rejections of 112/1st and 2nd paragraphs, particularly for the "prophylactic treatment" which has been cancelled. However, they have not overcome the rejection of 112/1st paragraph for the scope of diseases covered by the action of phosphodiesterase isoenzyme.

Claims 1-42, 49 and 50 are cancelled.

Claims 43-48 and 51-59 are pending.

Claim Rejections - 35 USC § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

1. **Scope of Enablement:** Claims 43, 46-48 and 51-59 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating asthma or COPD, does **not** reasonably provide enablement for a method of treating other diseases related to phosphodiesterase isoenzyme. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The following factors have been considered in the determination of an enabling disclosure:

- (1) The breadth of the claims;
- (2) The amount of direction or guidance presented;
- (3) The state of the prior art;
- (4) The relative skill of those in the art;
- (5) The predictability or unpredictability of the art;
- (6) The quantity of experimentation necessary;

[See *Ex parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Int., 1986); also *In re Wands*, 858 F. 2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988)].

The breadth of the claims: Claim 43 recites: "A method for the treatment of a disease...characterized by being amenable to treatment with a phosphodiesterase inhibitor..." which covers not only asthma and COPD, but also other diseases such as those listed in the specification, see the following excerpt:

[0114] Compounds of the present invention are useful as inhibitors of phosphodiesterase isoenzymes. The compounds or compositions of the present invention may be used to prevent or treat any disease in which the compounds or compositions are useful, but particularly a disease in which raising the intracellular concentration of cAMP is desirable. Examples of diseases against which compounds are useful include respiratory disorders including, in particular, asthma, bronchitis, chronic obstructive pulmonary disease (COPD), adult respiratory distress syndrome (ARDS), allergic asthma, hay fever, allergic rhinitis, and cystic fibrosis. They may also be used topically in skin disorders such as atopic dermatitis or psoriasis, ocular inflammation, or any other disease including cerebral ischaemia or auto-immune diseases in which increasing intracellular concentrations of cAMP is considered benefi-

Claim 53 recites: "A method of treating a mammal in need of a smooth muscle relaxant and/or anti-inflammatory compound..." Note, the term "inflammation" covers the treatment of a wide range of diseases such as: asthma, COPD, arthritis, otitis media, cystitis, blepharitis, conjunctivitis, allergic reaction, ulcers, cholecystitis, etc. That is, said term covers any disease which involves the recruitment of neutrophils, activation of T- and B-lymphocytes, macrophages, eosinophils and/or fibroblasts as well as the infiltration of tissue with mononuclear inflammatory cells.

Thus, the scope of claims 43, 53 and dependents thereon are unduly broad.

The amount of direction or guidance presented: The specification only provides evidence for the treatment of asthma and COPD. It does not provide data for the treatment of other diseases such as: arthritis, various infection (e.g., otitis media), autoimmune diseases, psoriasis, cerebral ischemia, etc. Thus, the specification fails to provide evidence to support the treatment of diseases other than asthma and COPD.

The state of the prior art: As mentioned in the previous action, the claimed tricyclic core is known to treat cardiovascular disorder, particularly hypertension. No reference correlates said core to the treatment of asthma, COPD, ocular inflammation, cerebral ischemia, etc. Furthermore, many commercial drugs have only one indication, and might even be contraindicated in other diseases. For example, Ibuprofen (an NSAID) can treat arthritis (an inflammatory disorder), but is contraindicated in asthma (another inflammatory disorder). Thus, the mere fact that a compound has anti-inflammatory activity does not mean it can treat a whole array of inflammatory disorders.

The relative skill of those in the art: Even with the advanced training, the skilled clinician would have to carry out extensive research to select an effective compound from the large Markush group of formula I. Not only one has to determine an IC₅₀ value, but also *in-vivo* activity to establish an LD₅₀, therapeutic index and pharmacokinetic profile for each compound. Given a large Markush group of the claimed formula I, such a task would require a tremendous amount of effort, time and resource.

The predictability or unpredictability of the art & The quantity of experimentation necessary: The pharmaceutical art has been known for its unpredictability due to various conflicting path ways, or biological factors that are sometimes genetically unique to individuals. In the instant case, the specification only demonstrates the activity for treating asthma and COPD, which is not sufficiently enable the skilled clinician to treat the many diseases that are allegedly related to phosphodiesterase isoenzyme, particularly, PDE III and PDE IV.

See *Hoffman v. Klaus* 9 USPQ 2d 1657, and *Ex parte Powers* 220 USPQ 925 regarding type of testing needed to support *in vivo* uses.

Thus, given the unpredictable nature of the art, and the vast number of compounds claimed herein, one skilled in the art will have to carry out undue experimentation to practice the method of treatment recited in claims 43, 46-48 and 51-59.

Recently, in *Rasmussen v. SmithKline Beecham Corp.* the court has commented that “where there is ‘no indication that one skilled in [the] art would accept without question statements [as to the effects of the claimed drug products] and no evidence has been presented to demonstrate that the claimed products do have those effects,’ an applicant has failed to

demonstrate sufficient utility and therefore cannot establish enablement.” [75 USPQ 2d, 1297, 1300].

Also, no compound has ever been found to treat diseases of all types generally. Since this assertion is contrary to what is known in medicine, proof must be provided that this revolutionary assertion has merits. Note, substantiation of utility and its scope is required when utility is “speculative”, or “sufficiently unusual”. See *Ex parte Jovanovics*, 211 USPQ 907, 909; *In re Langer* 183 USPQ 288. Also, see *Hoffman v. Klaus* 9 USPQ 2d 1657, and *Ex parte Powers* 220 USPQ 925 regarding type of testing needed to support *in vivo* uses.

Allowable Subject Matter

2. Claims 44, 45 and 60-63 are allowable because they are either directed to a method of treating asthma or COPD with a compound of formula I which is not taught or fairly suggested by the prior art of record.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37

CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tamthom N. Truong whose telephone number is 571-272-0676. The examiner can normally be reached on M, T and Th (9:00-5:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



Tamthom N. Truong
Examiner
Art Unit 1624

4-30-07



EMILIE L. BORCHARDT
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